

Access to Naloxone: Evidence-Based Overdose Response Strategy



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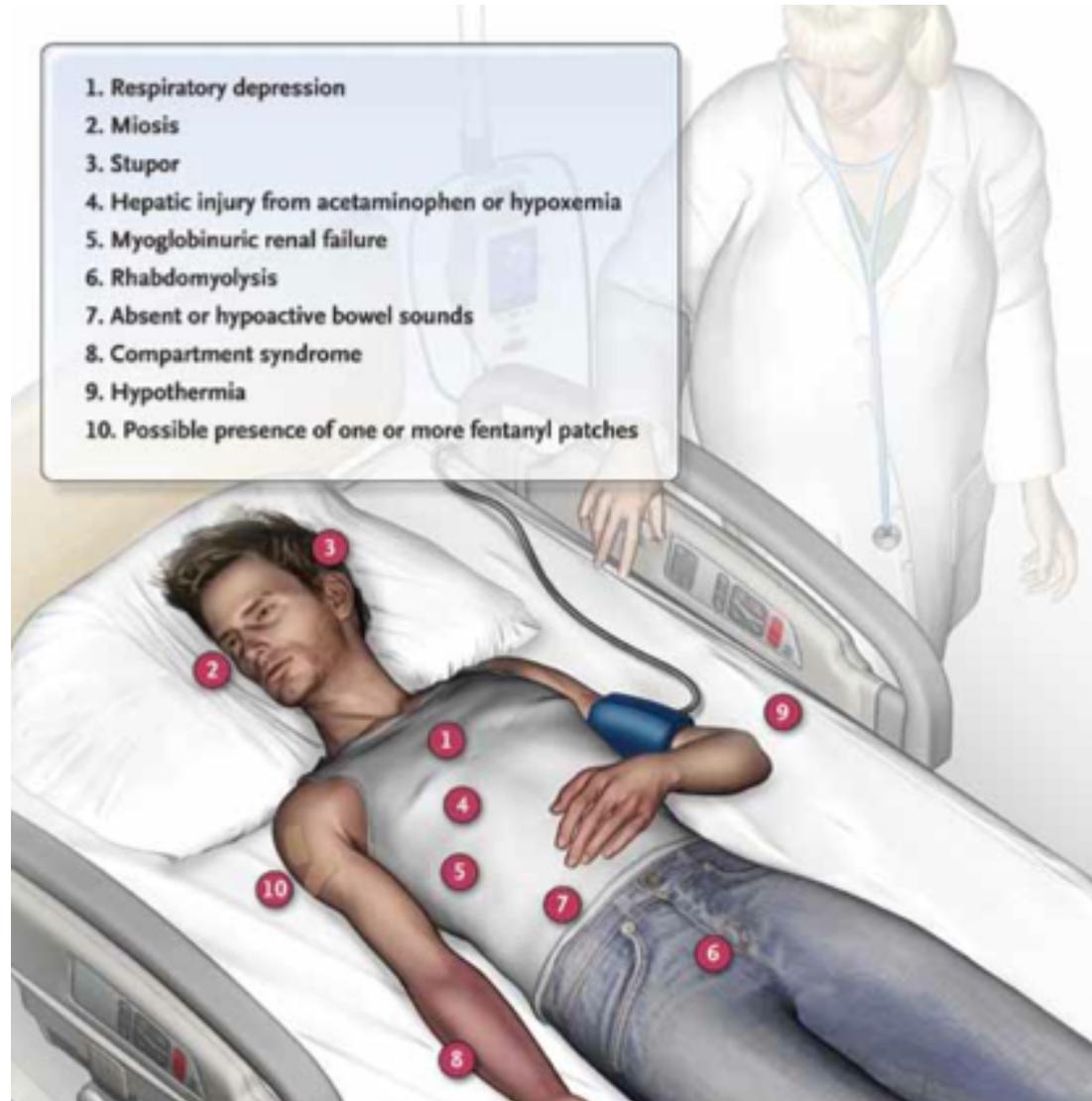
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Objectives

- 1) Identify strategies to prevent an opioid overdose
- 2) Understand the safety and efficacy of naloxone in reversing an opioid overdose
- 3) Describe how policies can be used to expand access to naloxone

Defining An Opioid Overdose

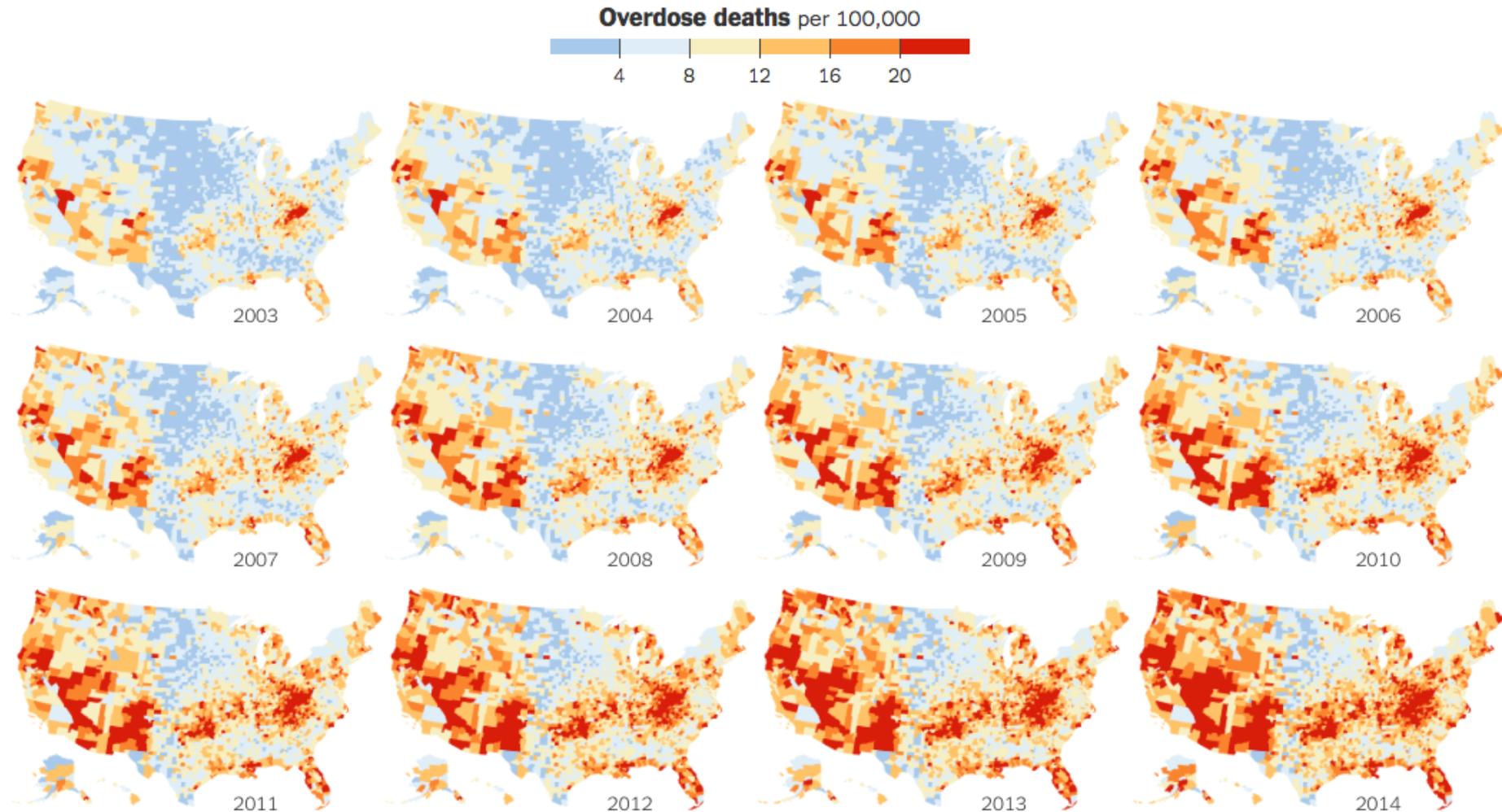
- Hallmark symptom of an opioid overdose is respiratory depression
- Respiratory depression defined as <13 breaths per minute
- Signs of opioid toxicity: apnea, stupor, and miosis



Drug Overdose

- According to the CDC, there is an epidemic of drug overdose fatalities
- Drug overdose is the leading cause of injury death in the U.S., surpassing deaths from motor vehicle accidents in 2007
- Prevalence among drug users: 73% have witnessed an overdose & 45% experienced a non-fatal overdose
- In long-term follow-up studies of patients who received addiction treatment, overdose is a leading cause of death
- Overdose is estimated to cost \$20.4 billion in 2009

Overdose Deaths in U.S.



States with Highest Rates of Overdose (2014)

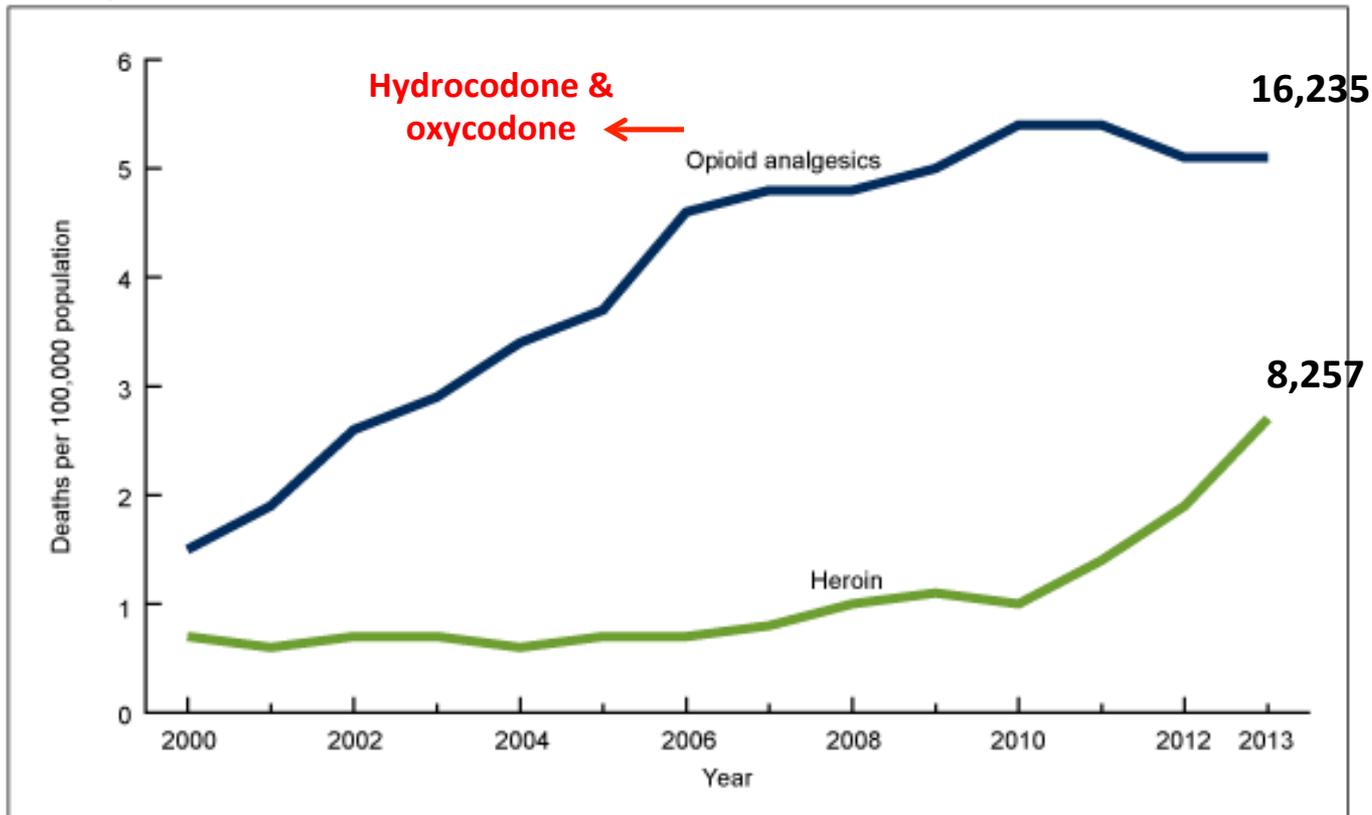
1. West Virginia (35.5 deaths per 100,000)
2. New Mexico (27.3)
3. New Hampshire (26.2)
4. Kentucky (24.7)
5. Ohio (24.6)

2014 had the highest rate of overdose fatalities ever recorded in the United States

Causes of Overdoses

- 74% were deemed unintentional & 17% were suicides
- Approximately 61% of overdose deaths involved an opioid

Figure 1. Age-adjusted rates for drug-poisoning deaths, by type of drug: United States, 2000–2013



Fentanyl-related Deaths

- In 2013 there were 84 fentanyl-related overdoses in Ohio, in 2014 that number grew to 502

Table 1: Top 10 states by total Fentanyl Seizures, 2014, unpublished NFLIS data

Rank	State	Number of Fentanyl seizures
1	Ohio	1245
2	Massachusetts	630
3	Pennsylvania	419
4	Maryland	311
5	New Jersey	238
6	Kentucky	232
7	Virginia	222
8	Florida	183
9	New Hampshire	177
10	Indiana	133

Heroin Adulterants & Diluents

- Benzodiazepines
- Cocaine
- Procaine – local anesthetic
- Quinine – antiparasitic (treats Malaria)
- Caffeine - stimulant
- Paracetamol – acetaminophen
- Lidocaine - anesthetic/antiarrhythmic
- Mannitol - diuretic
- Lactose - filler
- Starch - filler
- Dextrose - filler
- Diphenhydramine/Caffeine - Antihistamine
- Diphenhydramine/Thiamine

Novel Synthetic Opioids:

- ✓ Fentanyl
- ✓ Fentanyl analogs
- ✓ W-18
- ✓ U-4700
- ✓ AH-7921
- ✓ MT-45

Ask local toxicologist/coroners for local data

Risk Factors for Fatal Rx Opioid Overdose

Demographic

- Male
- Middle-aged (Rx opioids: 45-54 yrs; heroin: 25-34 yrs)
- Living in non-metropolitan areas (Heroin metro areas)
- Low-income (RR: 2.1-5.7)
- Non-Hispanic white

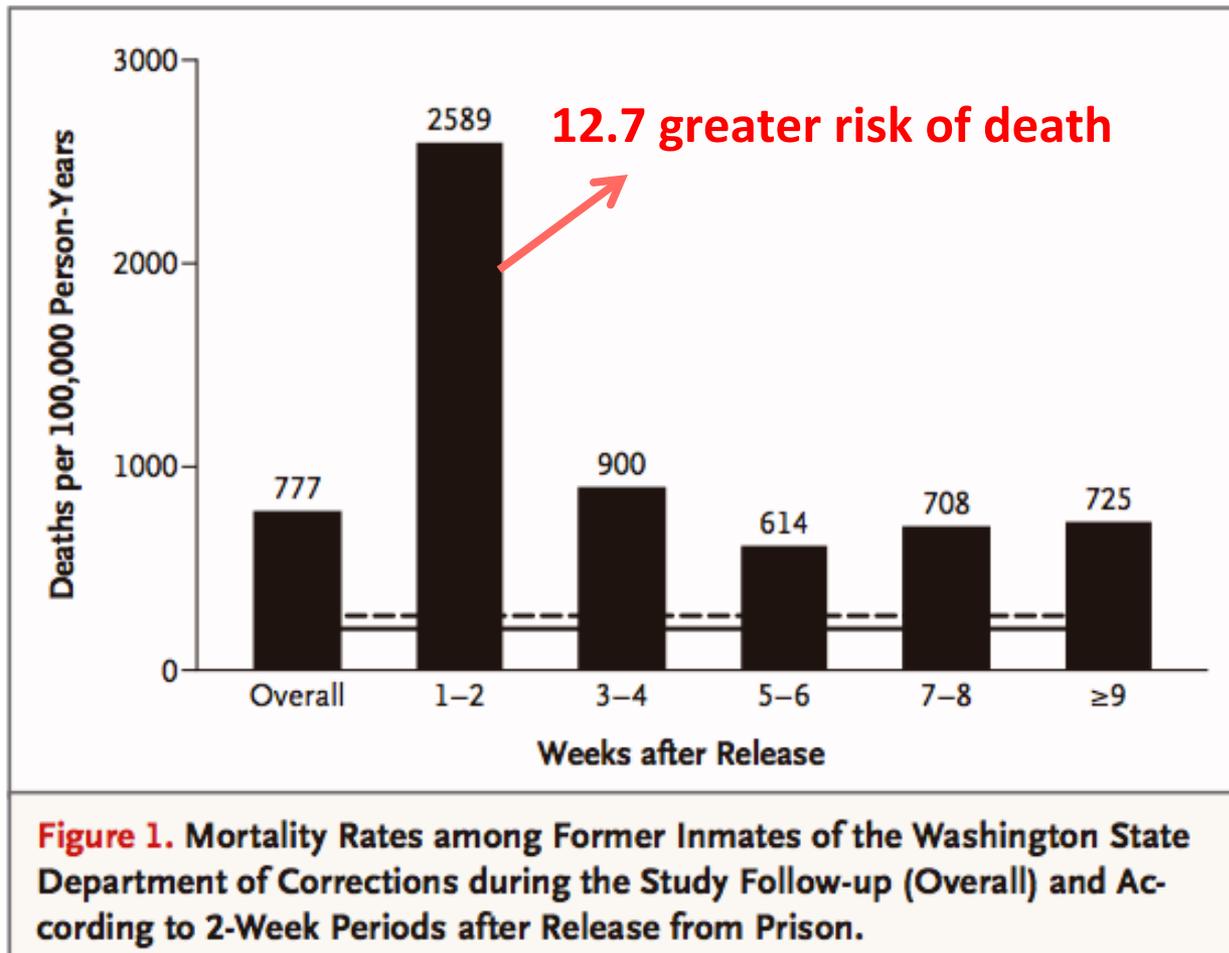
Physical Health

- History of chronic pain (82%)
- Having a prescription (75% prescription opioid vs 29% for methadone)
- Signs of non-medical use (51%)
- Greater number of prescribers (RR: 2.8)
- Greater number of prescriptions (RR: 8.2)
- High daily dose (>80 mg morphine equivalent dose)

Behavioral Health

- History of substance abuse (60-78%)
- History of mental illness (42-57%)
- IV drug use (22%)
- Previous overdose (17%)

Drug Overdose is the Leading Cause of Death Among Former Inmates



OVERDOSE PREVENTION

Overdose Education Delivery

- Delivery:
 - 1:1 in-person
 - Group 
 - Video
 - Educational materials/brochures
- Length varies from 10-60 minutes
- May be legislative requirements that overdose prevention education is required to distribute naloxone

Good to discuss
ineffective responses to
overdose

Symptoms of an Opioid Overdose

- Breathing is slow & shallow or has stopped
- Vomiting
- Face is pale & clammy
- Blue or grayish lips & fingernails
- Slow, erratic or no pulse
- Choking or loud snoring noises (“death rattle”)
- Will not respond to shaking or sternum rub
- Skin may turn gray, blue or ashen

Overdose Prevention

- Do not mix opioids, benzodiazepines & alcohol
- People who have stopped using for a period of time & try to use again
- Quality & adulterants (for example, fentanyl)
- Using alone
- Make an overdose plan with a friend
- Age & physical health (for example, respiratory problems like asthma or COPD)
- Learn to recognize overdose as decreased respiration
- Call 911 and administer naloxone

Education on Fentanyl

What is fentanyl?

- Fentanyl is a fast-acting synthetic opioid that is at least 20 times **MORE POTENT THAN HEROIN**
- Fentanyl is currently responsible **for 20% of all overdose deaths** in Ohio
- The fentanyl killing people is being **illegally** produced and cut into, or sold as heroin
- There is **NO WAY TO TELL HOW TOXIC** the drug is going to be-even the dealer doesn't know

For fentanyl overdoses, **YOU NEED MORE NARCAN!**

- While Narcan (naloxone) reverses an overdose, if fentanyl is on board, 1 or 2 doses is **NOT** enough
- If you witness and overdose, **CALL 911 FIRST, THEN USE NARCAN**
- Seek medical help even if the person is revived
- Narcan usually wears off before the drug does, **A PERSON CAN STILL DIE!**

When is it an Overdose?

REALLY HIGH	versus	OVERDOSE
Muscles become relaxed		Pale, clammy skin
Speech is slowed/slurred		Very infrequent or no breathing
Sleepy looking		Deep snoring or gurgling
Nodding but will respond to stimulation like yelling, sternal rub, pinching, etc.		Heavy nod, not responsive to stimulation
		Slow or no heart beat/pulse

Responses to an Overdose

- Clients may have misunderstanding of how to respond to an overdose
- Anecdotal experiences that have worked to reverse an overdose
- Unresponsive person requires stimulus

Overdose Response	Percent (Number)
Called 911	34.6% (n=47)
Other	18.4% (n=25)
Nothing	9.6% (n=13)
Cold water or ice	8.1% (n=11)
Transported to hospital	5.9% (n=8)
CPR & called 9-1-1	5.9% (n=8)
Initiated CPR	4.4% (n=6)
Rescue breathing & 9-1-1	4.4% (n=6)
Slapped or hit	4.4% (n=6)
Administered naloxone	2.2% (n=3)
Rescue breathing	1.5% (n=2)
Sternum rub & CPR	0.7% (n=1)

76% of clients had witnessed or experienced an overdose, but only 53% had heard of naloxone

Overdose Education Among Drug Users

Among clients in addiction treatment for opioid use disorders, overdose prevention education largest improvements in:

- Sternum rub (52% improvement)
- Placing people in the recovery position (37%)
- Not giving stimulants (29%)
- Snore-like gurgling noise symptom of overdose (29%)
- Perform rescue breathing (27%)
- Do not walk someone around the room (25%)
- Administer naloxone (24%)
- Do not inject them with saline or water (22%)

Overdose Reversal

- Naloxone hydrochloride (brand name Narcan), FDA-approved in 1971, is a short-acting competitive mu opioid-receptor antagonist, and the only agent that can *reverse* an opioid overdose
- First synthesized in 1960
- Well-established efficacy and safety
- Used by EMS & hospitals for over 40 years
- Very specific mechanism of action
- Dose up to 700/x recommended dose without seeing adverse events



Naloxone Dosing

Medical setting:

- Recommended start 0.04mg, increase every 2-3 minutes at rate 0.5mg, 2mg, 4mg, 10mg, 15 mg – until adequate respiration
- Onset within 2 minutes, duration 20-90 minutes; administered IV/IM/IO/IN
- Observe 4-6 hours standard, at least 8 hours if long-acting opioid used (methadone, fentanyl patch)

Community setting:

- Two doses per client
- More doses may be necessary in areas where heroin is known to be adulterated with fentanyl

Naloxone Side Effects?

- Confusion
 - Headache
 - Gastrointestinal problems
 - Aggressiveness
 - Tachycardia
 - Shivering
 - Sweating
 - Tremor
 - Seizures
 - Naloxone sensitivity
 - Cardiac arrest
 - Pulmonary edema
 - Renarcotization
- Many symptoms thought to be attributable to naloxone result from opioid withdrawal
 - Long-term drug use may increase the probability of an adverse event (AE), reflecting an underlying morbidity –NOT naloxone AE

Naloxone Administration

- FDA approved IV/IM administration of naloxone
- April 2014 FDA approved auto-injector (0.4mg/0.4mL) Evzio (~\$575) with audio instructions
- November 2015 FDA approved a nasal device (4mg/1mL) from Adapt Pharma (\$75)



Naloxone Cost Effectiveness

- Based on naloxone distribution to 20% of heroin users
- Estimated 6% overdose deaths averted
- 1 save per 227 naloxone kits distributed
- Incremental cost \$53
- Each death prevented by distribution of naloxone kits will cost \$438 (ICER)
- **HIGHLY COST EFFECTIVE**

Mode of Naloxone Administration

COMMENTARY

Tangled-up and blue: releasing the regulatory chokehold on take-home naloxone

Naloxone is the most proximal intervention that we have to reduce premature mortality associated with unintentional opioid overdoses and it has been demonstrated to be highly efficacious, safe and cost-effective. The effectiveness of naloxone formulations may vary depending on the setting and the person responding to the overdose.

Mode of Naloxone Administration

Nasal naloxone or Auto-Injector:

- Non-drug users without medical training
- People in recovery from opioid addiction, avoid needle as a potential “trigger”

Intramuscular:

- Individual with medical training
- Active injection drug users
- Particularly important if heroin known to be adulterated with fentanyl

Intramuscular/IV:

- Medical settings only (ambulance, emergency department)
- Particularly important if heroin known to be adulterated with fentanyl

Overdose Prevention

The only evidenced-based intervention that has demonstrated to *prevent* heroin overdose, is medication assisted treatment with methadone or buprenorphine

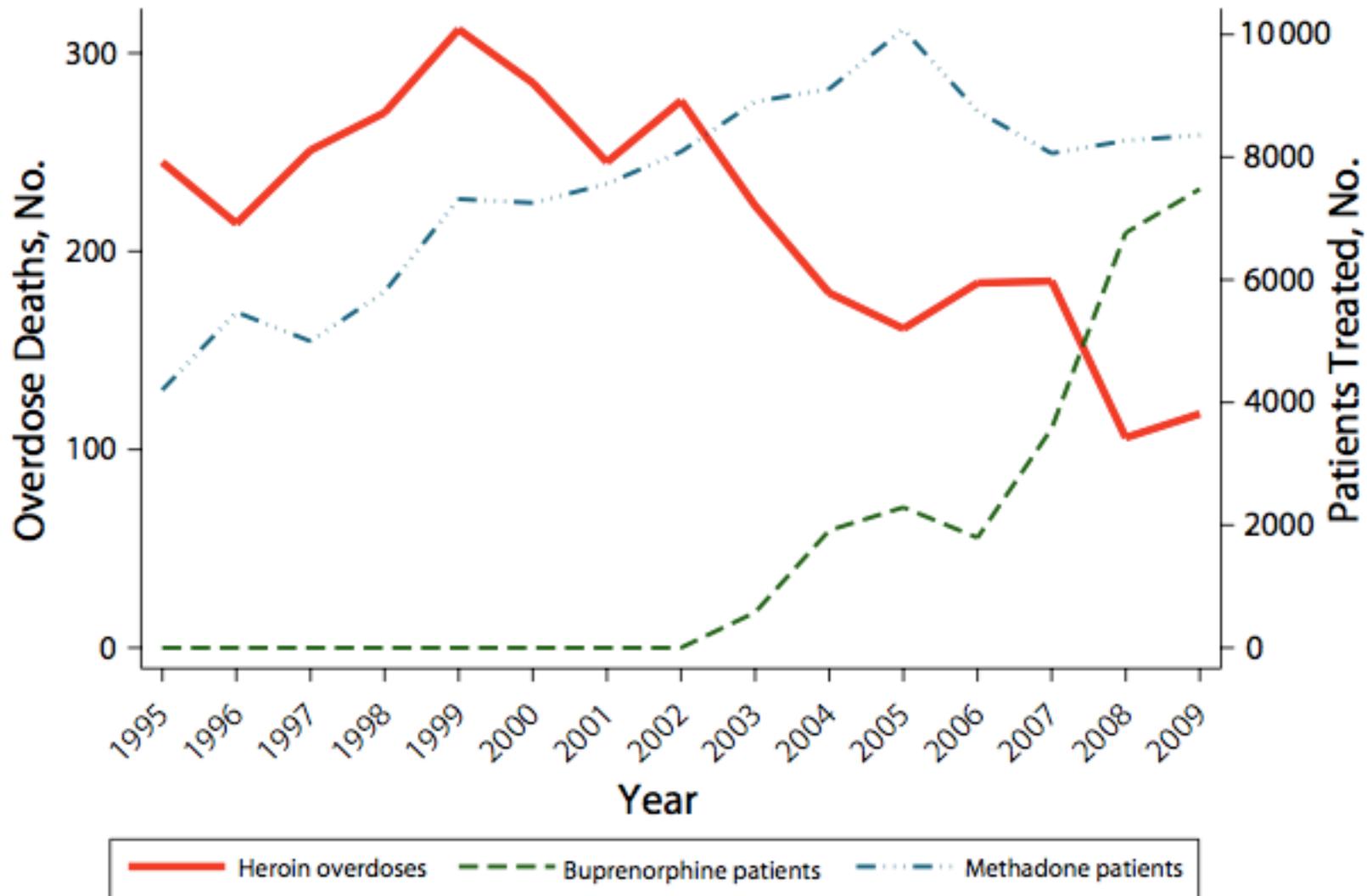


FIGURE 1—Heroin overdose deaths and opioid agonist treatment: Baltimore, MD, 1995-2009.

SOURCES: Schwartz et al. (2013) *American Journal of Public Health*

Opioid Overdose Prevention Programs

Began in 1996 & the key components are:

- 1) training on how to identify the symptoms of an opioid overdose
- 2) how to respond, including administration of naloxone (bystander administration)

Why important:

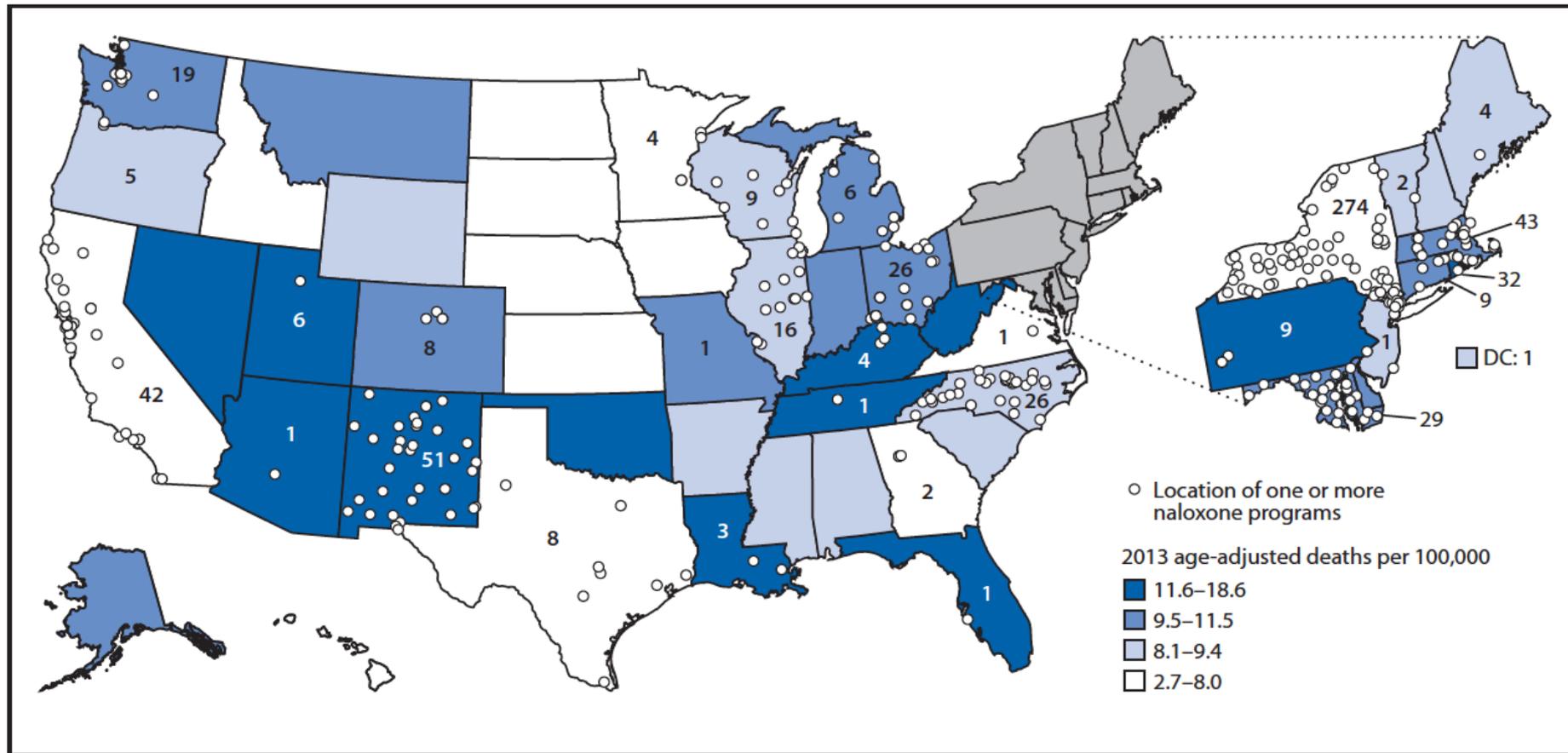
- Many people don't call 911
- EMT-Basics & first responders can not administer naloxone in some jurisdictions
- In rural Ohio, it can take EMS 17-18 minutes to respond

SOURCES: *Sporer & Kral 2007; Enteen et al. 2010; Baca & Grant 2007*



Distribution of OOPPs by State

FIGURE 2. Number* and location of local drug overdose prevention programs providing naloxone to laypersons, as of June 2014, and age-adjusted rates† of drug overdose deaths§ in 2013 — United States



* Total N = 644; numbers on map indicate the total number of programs within each state.

† Per 100,000 population.

§ CDC, National Center for Health Statistics; Compressed Mortality File 1999-2013 on CDC WONDER Online Database, released January 2015.

Review of OOPPs

- 1) Lay persons can and will administer naloxone
- 2) Overdoses are common among active drug users, as well as people seeking treatment for drug use disorders
- 3) Mixed evidence regarding whether people, as a result of overdose education, are more likely to call 9-1-1
- 4) No evidence to suggest that naloxone encourages drug use
- 5) Non-medical persons can increase their knowledge of the signs and symptoms of an overdose

REVIEW

A Systematic Review of Community Opioid Overdose Prevention and Naloxone Distribution Programs

Angela K. Clark, MSN, RN, Christine M. Wilder, MD, and Erin L. Winstanley, PhD

OOPPs in Ohio

Table 1: Descriptive Characteristics of OOPPs

	%(N)
OOPP Location	
Rural	17.4 (4)
Suburban	47.8 (11)
Urban	34.8 (8)
Target population	
Patients in addiction treatment	77.8 (14)
Persons actively using illicit drugs	88.9 (16)
Family members	88.9(16)
Funding sources	
Ohio Department of Health	33.3 (6)
Interact for Health	16.7 (3)
Terminal distributors license	64.7 (11)
Frequency of Overdose Education	
On demand/as needed	55.6 (10)
Daily	11.1 (2)
Monthly	22.2 (4)
Overdose education format	
Individual only	22.2 (4)
Group only	27.8 (5)
Individual & group	50.0 (9)
Experienced any implementation barriers or problems	52.6 (10)
Experienced problems gaining buy-in	27.8 (5)
Barriers to providing overdose prevention services in Ohio	64.7 (11)

Barriers to OOPPs Implementation

Table 2: OOPP Implementation Barriers*

Stigma (n=14)	<ul style="list-style-type: none"> • Community buy-in • Perceive naloxone as a safety net or enabling opioid use • Medical professionals buy-in • Internal staff or board member buy-in • Stakeholder buy-in
Cost (n=7)	<ul style="list-style-type: none"> • Medication • Medical staff time • Payor reimbursement non-medication items in kit
Staffing (n=5)	<ul style="list-style-type: none"> • Nursing and physician staff and/or time to write prescriptions for naloxone
Legal (n=4)	<ul style="list-style-type: none"> • Law enforcement confiscate overdose kits • Believe that people are trading naloxone for heroin • Buy-in from law enforcement or judicial system
Regulatory (n=3)	<ul style="list-style-type: none"> • Need for standing orders • Lack of clarity regarding how regulations inform organizational policies & procedures
Clients (n=3)	<ul style="list-style-type: none"> • Location of program • Some patients do not want overdose kits • Lack of participation due to legal fears

* This table contains a summary of the responses to the open-ended question regarding the barriers or problems the organization experienced in providing overdose prevention services.

Improving & Expanding Overdose Prevention

- Affordability & access to naloxone
- Point-of-care distribution of naloxone
- Tailoring education to different at-risk populations
- Co-prescribing of naloxone for persons: 1) high dose of opioids, 2) co-prescribed benzodiazepines, & 3) opioids + antidepressants
- Medication safety for all patients receiving opioids
- Outreach & education for active drug users (e.g., syringe exchange programs)
- Increase access to medications to treat opioid use disorders
- Naloxone distribution to all patients leaving AMA from residential addiction treatment programs



POLICY ISSUES

Legal Issues in Prescribing/ Administering Naloxone

Jurisdiction has a naloxone law

Prescribers immune from criminal liability

Prescribers immune from civil liability

Third party prescription authorized

Prescription by standing order authorized

Lay administrator immune from criminal prosecution

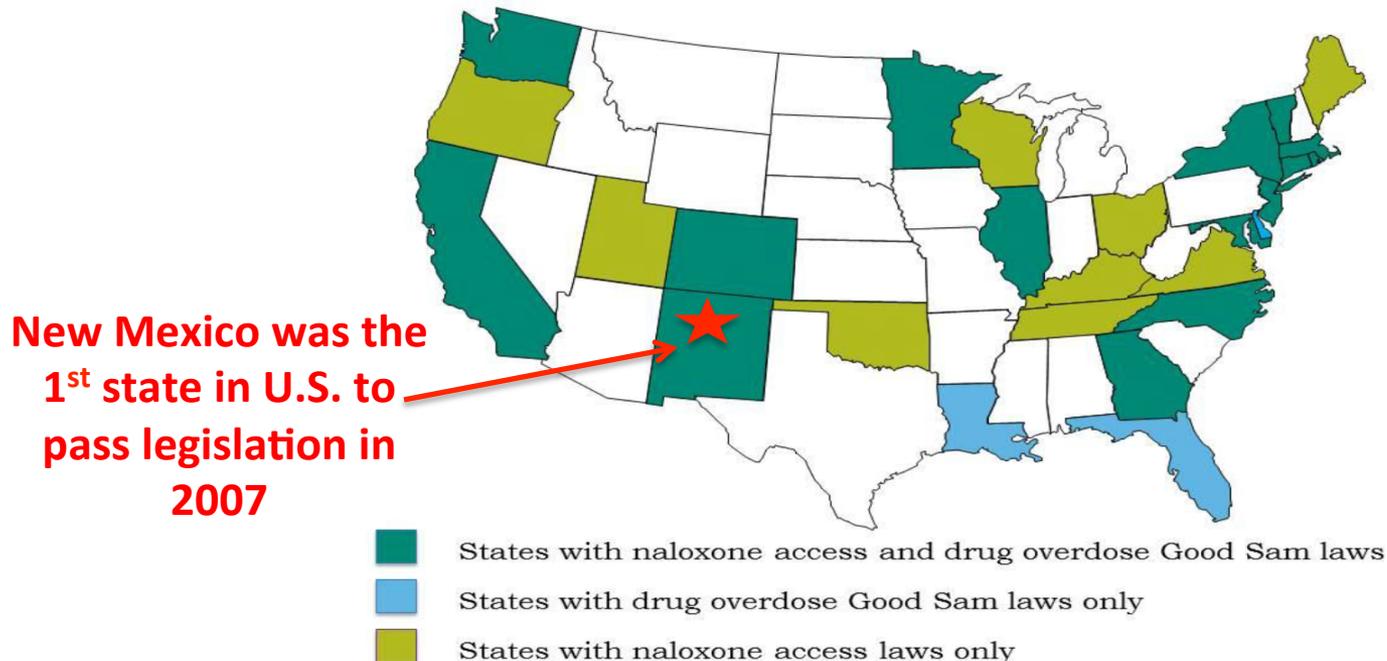
Lay administrator immune from civil liability

Removes criminal liability for possession of naloxone

Legal Issues

State-level variation in whether:

1. Immunity for person who calls 9-1-1 and/or administers naloxone
2. Civil & criminal protections for physicians that prescribe naloxone
3. Protection for lay persons carrying naloxone



Regulatory Issues

- Basic level first responders may not be able to administer IV/IM medications which is particularly problematic in rural areas
- Some states do not allow naloxone to be prescribed to a third party
- Rhode Island Board of Pharmacy approved a collaborative prescription agreement
- Massachusetts expanded access by using a standing order

Rhode Island makes lifesaving overdose drug easily available

Published: February 15, 2014 10:32 PM

Comments 6



An overdose kit containing injectable naloxone is \$25.

bob thayer/the providence journal

Ohio HB 4

- Expanded access to naloxone
 - 3rd party prescribing
 - Pharmacies can adopt a standing order to provide naloxone to community members without a prescription

Myths Versus Facts

Myth: People will use more heroin because they know Narcan can be used to save them if they overdose.

Fact: People will use heroin whether or not Narcan is available. The majority of people using drugs do not want to die, they are struggling with addiction. Administering Narcan means that someone may have another chance to enter treatment.

Concluding Remarks

- Overdose is a preventable cause of death
- Education & provision of MAT can prevent an overdose from occurring
- Naloxone is a safe, efficacious and cost-effective medication that can prevent an overdose fatality
- Further regulatory and legal changes are needed to expand access to naloxone & ensure 911 is called

